IN THE SPECIFICATION

Please add the following paragraph immediately after the title on page 1.

B1

This application is a national stage application filed under 35 U.S.C. § 371 of International Application No. PCT/US99/11497, filed May 25, 1999 and published in English as WO 99/61614 on December 2, 1999, which claims the benefit of U.S. Provisional Application No. 60/087,104, filed May 28, 1998, and U. S. Provisional Application No. 60/150,701, filed December 17, 1998.

Please replace the paragraph beginning at page 3, line 21, with the following rewritten paragraph:

B2

The invention features substantially purified polypeptides, human SOCS proteins, referred to collectively as "HSCOP" and individually as "HSCOP-1", "HSCOP-2", "HSCOP-3", "HSCOP-4", "HSCOP-5", "HSCOP-6", "HSCOP-7", "HSCOP-8", and "HSCOP-9". In one aspect, the invention provides a substantially purified polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-9, and fragments thereof.

Please replace the paragraph beginning at page 21, line 21, with the following rewritten paragraph:

B3

The nucleotide sequences of the present invention can be engineered using methods generally known in the art in order to alter HSCOP-encoding sequences for a variety of purposes including, but not limited to, modification of the cloning, processing, and/or expression of the gene product. DNA shuffling by random fragmentation and PCR reassembly of gene fragments and synthetic oligonucleotides may be used to engineer the nucleotide sequences. For example, oligonucleotide-mediated site-directed mutagenesis may be used to introduce mutations that create new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, and so forth.

Please replace the paragraph beginning at page 32, line 2, with the following rewritten paragraph:

In addition, techniques developed for the production of "chimeric antibodies," such as the splicing of mouse antibody genes to human antibody genes to obtain a molecule with appropriate antigen specificity and biological activity, can be used. (See, e.g., Morrison, S.L. et al. (1984) Proc. Natl. Acad. Sci. 81:6851-6855; Neuberger, M.S. et al. (1984) Nature 312:604-608; and Takeda, S. et al. (1985) Nature 314:452-454.) Alternatively, techniques described for the production of single chain antibodies may be adapted, using methods known in the art, to produce HSCOP-specific single chain antibodies. Antibodies with related specificity, but of distinct idiotypic composition, may be generated by chain shuffling from random combinatorial immunoglobulin libraries. (See, e.g., Burton D.R. (1991) Proc. Natl. Acad. Sci. 88:10134-10137.)

Please replace the paragraph beginning at page 32, line 31 and ending on page 33, line 16, with the following rewritten paragraph:

Various methods such as Scatchard analysis in conjunction with radioimmunoassay techniques may be used to assess the affinity of antibodies for HSCOP. Affinity is expressed as an association constant, K_a, which is defined as the molar concentration of HSCOP-antibody complex divided by the molar concentrations of free antigen and free antibody under equilibrium conditions. The K_a determined for a preparation of polyclonal antibodies, which are heterogeneous in their affinities for multiple HSCOP epitopes, represents the average affinity, or avidity, of the antibodies for HSCOP. The K_a determined for a preparation of monoclonal antibodies, which are monospecific for a particular HSCOP epitope, represents a true measure of affinity. High-affinity antibody preparations with K_a ranging from about 10^9 to 10^{12} L/mole are preferred for use in immunoassays in which the HSCOP-antibody complex must withstand rigorous manipulations. Low-affinity antibody preparations with K_a ranging from about 10^6 to 10^7 L/mole are preferred for use in immunopurification and similar procedures which ultimately require dissociation of HSCOP, preferably in active form, from the antibody (Catty, D. (1988) Antibodies, Volume I: A Practical Approach, IRL Press, Washington, DC; Liddell, J. E. and Cryer, A. (1991) A Practical Guide to Monoclonal Antibodies, John Wiley & Sons, New York NY).

Please replace the paragraph beginning at page 33, line 17, with the following rewritten paragraph:

B6 The titer and avidity of polyclonal antibody preparations may be further evaluated to determine the quality and suitability of such preparations for certain downstream applications. For example, a polyclonal antibody preparation containing at least 1-2 mg specific antibody/ml, preferably 5-10 mg specific antibody/ml, is preferred for use in procedures requiring precipitation of HSCOP-antibody complexes. Procedures for evaluating antibody specificity, titer, and avidity, and guidelines for antibody quality and usage in various applications, are generally available. (See, e.g., Catty, supra, and Coligan et al. supra.)

Please replace the paragraph beginning at page 46, line 14, with the following rewritten paragraph:

B7 Without further elaboration, it is believed that one skilled in the art can, using the preceding description, utilize the present invention to its fullest extent. The following preferred specific embodiments are, therefore, to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever.

Please replace the paragraph beginning at page 46, line 18, with the following rewritten paragraph:

B8 The entire disclosure of all applications, patents, and publications, cited above and below, and of US provisional applications 60/087,104 (filed May 28, 1998), and 60/150,701 (filed December 17, 1998) are hereby incorporated by reference.

Please replace the paragraph beginning at page 53, line 23 and ending on page 54, line 1, with the following rewritten paragraph:

B9 Sequences complementary to the HSCOP-encoding sequences, or any parts thereof, are used to detect, decrease, or inhibit expression of naturally occurring HSCOP. Although use of oligonucleotides comprising from about 15 to 30 base pairs is described, essentially the same procedure is used with smaller or with larger sequence fragments. Appropriate oligonucleotides are designed using OLIGO 4.06 software (National Biosciences) and the coding sequence of

HSCOP. To inhibit transcription, a complementary oligonucleotide is designed from the most unique 5' sequence and used to prevent promoter binding to the coding sequence. To inhibit translation, a complementary oligonucleotide is designed to prevent ribosomal binding to the HSCOP-encoding transcript.

B9

Please replace the paragraph beginning at page 57, line 4, with the following rewritten paragraph:

Naturally occurring or recombinant HSCOP is substantially purified by immunoaffinity chromatography using antibodies specific for HSCOP. An immunoaffinity column is constructed by covalently coupling anti-HSCOP antibody to an activated chromatographic resin, such as CNBr-activated SEPHAROSE (Amersham Pharmacia Biotech). After the coupling, the resin is blocked and washed according to the manufacturer's instructions.

B10

Please replace the paragraph beginning at page 57, line 10, with the following rewritten paragraph:

Media containing HSCOP are passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of HSCOP (e.g., high ionic strength buffers in the presence of detergent). The column is eluted under conditions that disrupt antibody/HSCOP binding (e.g., a buffer of pH 2 to pH 3, or a high concentration of a chaotrope, such as urea or thiocyanate ion), and HSCOP is collected.

B11

IN THE CLAIMS

Please amend Claims 21, 22, 25, 29, 31, and 37 as follows.

For the Examiner's convenience, all pending claims are listed below. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."